

# UNAIDS

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## Translational HIV/AIDS research: past successes and futur challenges

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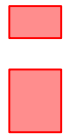
**anRS**

Agence nationale de recherches  
sur le sida et les hépatites virales



# 27 years of HIV translational science...

1983



Identification/Characterization of HIV-1 and viral antigens

Diagnostic Tests

First step for prevention and treatment

HIV target cells and HIV pathogenesis

Immune cell makers as prognosis and monitoring tests

Characterization HIV-1 replication cycle

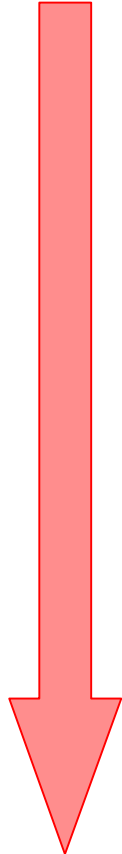
Drug discovery for prevention and therapy

HAART

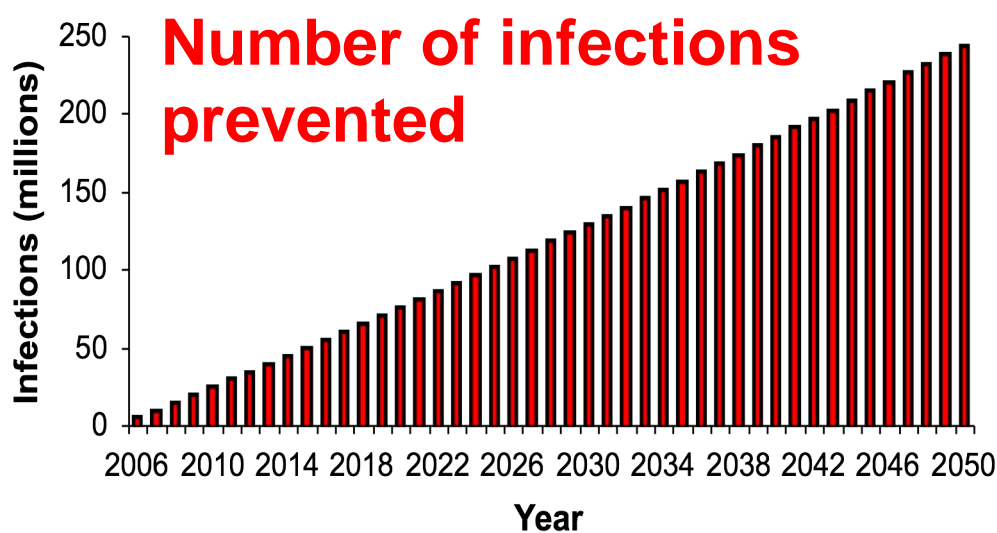
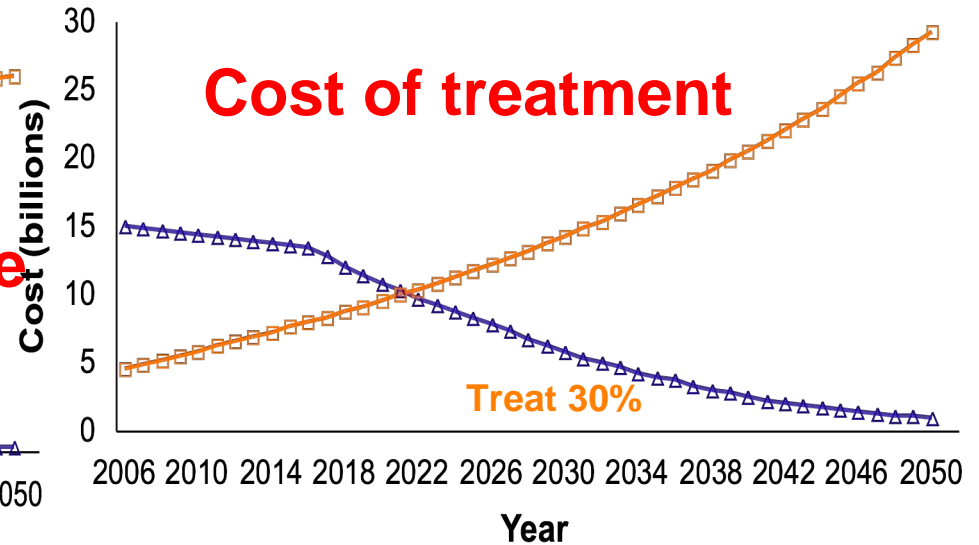
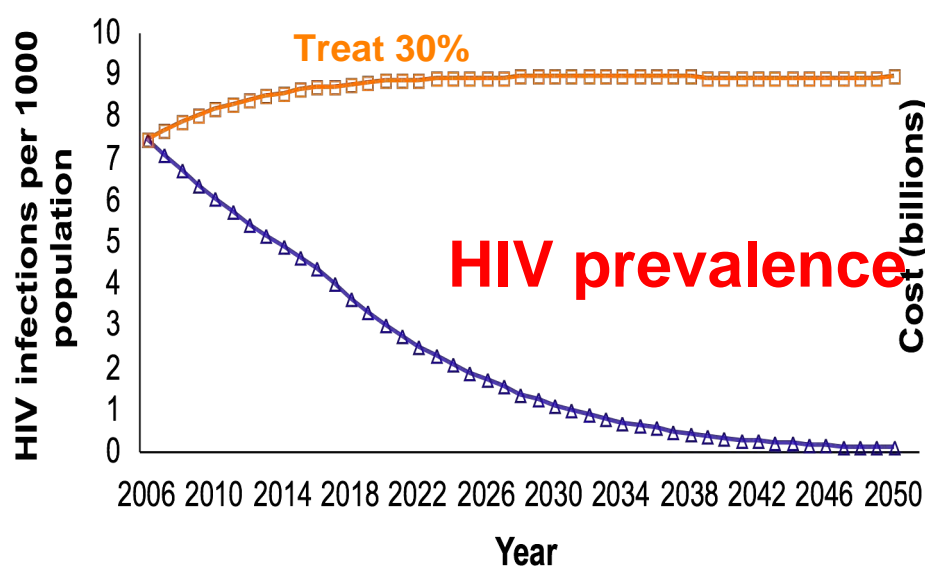
Characterisation HIV-1 genome and of its diversity

Monitoring tests for Viral load and ARV resistance

2010



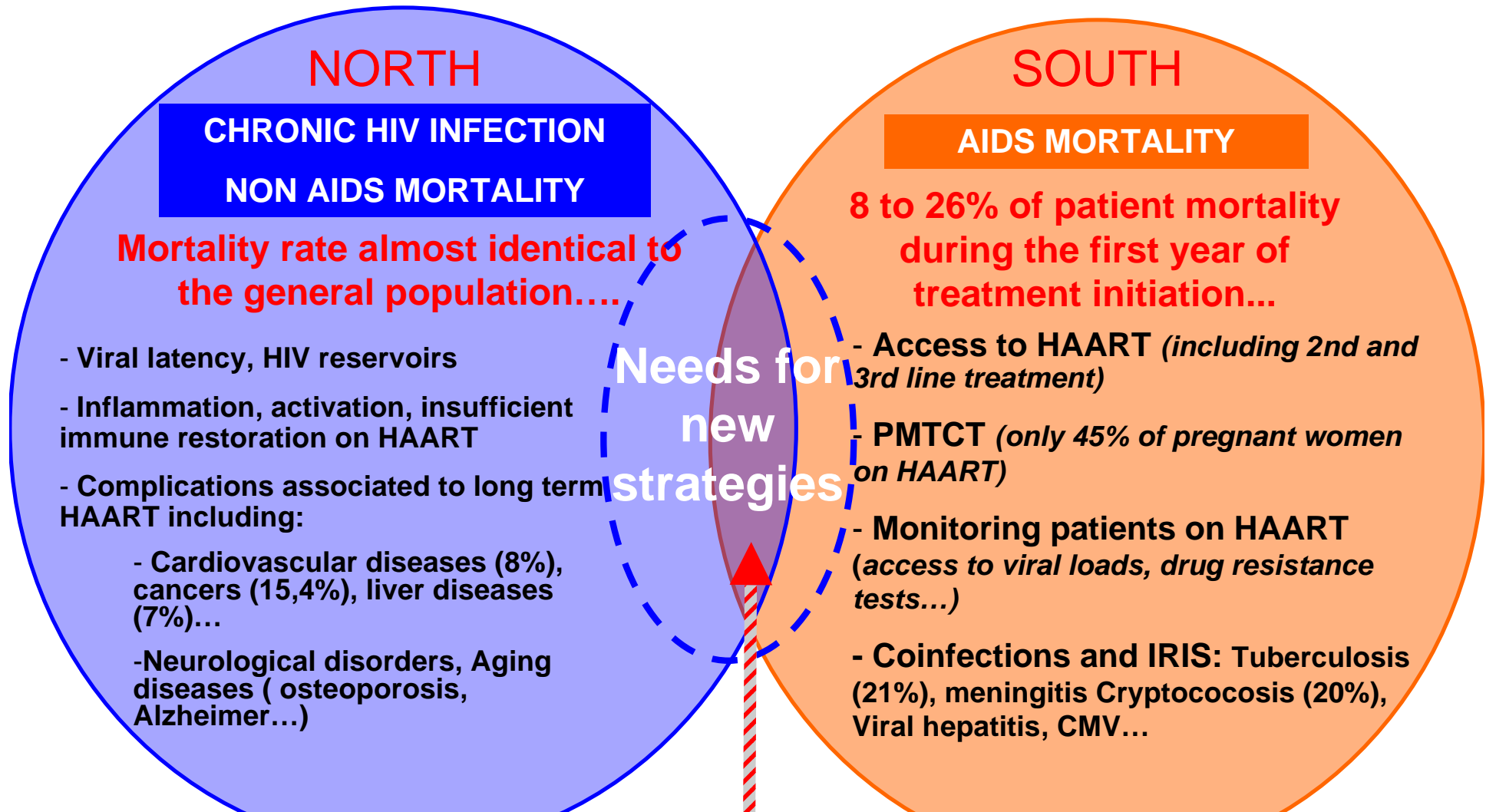
# The Power of HAART: Demographic Model



—△ Treat all      —□ Treat 30%

*Montaner et al, Lancet 2006*

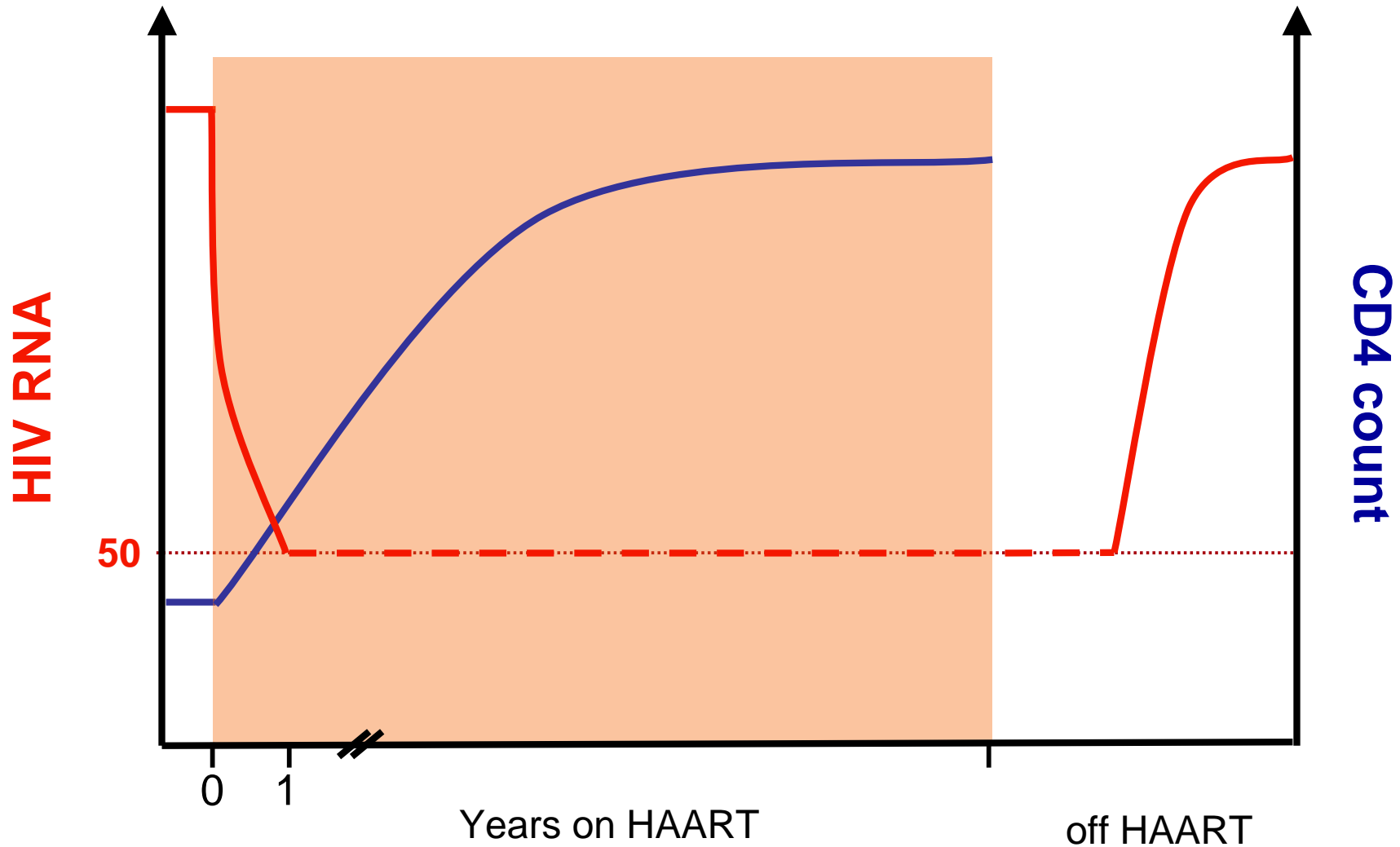
# Challenges in HIV/AIDS Research in 2010....



**Early Testing, Prevention (Microbicides? PreP? Vaccine?), Treatment (TasP?)**

**Needs for further international efforts and for further research for preventive and therapeutic strategies**

# Rapid rebound in virus when HAART stopped



# HIV reservoirs on HAART...

Very early establishment after the infection

**Which cells?** Predominantly  $T_{CM}$  et  $T_{TM}$  also monocyte/macrophages, astrocytes....

**Where?** Blood, Gut or brain (inaccessibility to drugs + high number of activated immune cells)

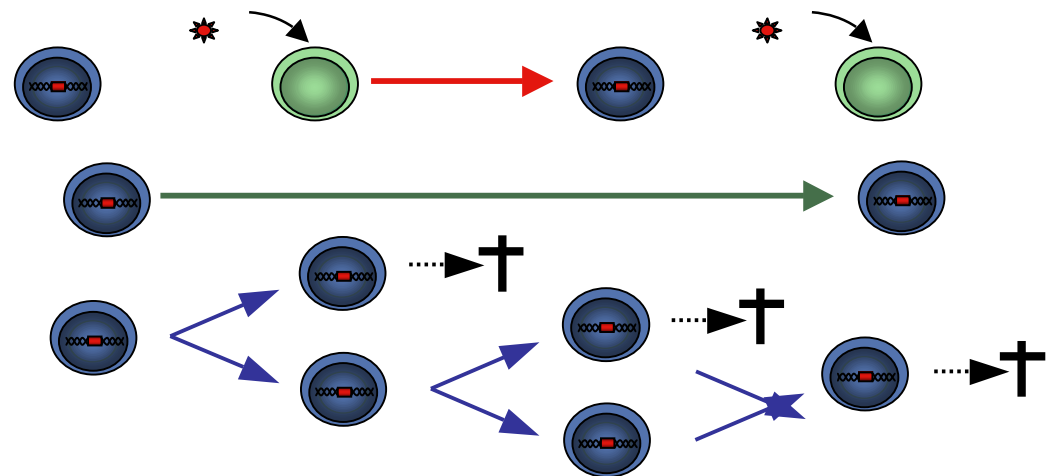
**Why?**

Viral replication

T cell survival

Proliferation

*Courtesy of Nicolas Chomont*



**How?**

# Potential strategies targeting HIV reservoirs

**Unlocking latency mechanisms** (*Histone deacetylase inhibitors, Vorinostat, methylation inhibitors like 5-aza-dC...*)

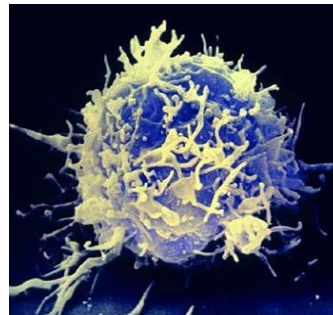
**Use of immunomodulating agent** (*cytokines like IL2, IL7, Maraviroc, PD1-antibody to target CD4 T<sub>CM</sub>...*) in HAART pts

**Enhancement of anti-HIV immunity** (*therapeutic immunization using DNA w/wo lipopeptides, rMVA, targeted DC....*)

**Antiretroviral drugs with improved penetration and potency** (*shRNA tat, rev, TAR..*)

**Intensifying antiretroviral treatment** (*raltegravir, dorunavir/r, Truvada..*)

**Early intense HAART** with *raltegravir, dorunavir/r, maraviroc* associated with *Truvada* in *primoinfected pts..(Optiprim)*



**Achieving functional cure?**

**Permanent suppression of viral replication without eradicating the virus from the body**

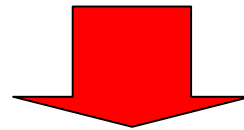
# Why it should be possible to obtain a functional cure for HIV/AIDS?

- A decrease in viral load is clearly associated with clinical benefit
- A small percentage (<0.3%) of HIV-1-infected subjects show no disease progression and/or spontaneous control of viral replication (*e.g. long-term nonprogressors and “HIV Controllers”*)
- African monkeys infected by SIV are naturally protected against disease progression



# Need for a Global Scientific Strategy on *Towards an HIV Cure...*

- The IAS decided to stimulate, coordinate and support a multidisciplinary working group to elaborate an International Scientific Strategy....



***A Global Scientific Consortium « Towards an HIV Cure » supported by International organizations in 2012?***



***With the support of the NIH, TAG, ANRS, SIDACTION...***

## Workshop Chair

2008 Nobel Laureate for Medicine and IAS Governing Council Member  
Françoise Barré-Sinoussi

The International AIDS Society is convening an invitation only, two-day workshop in advance of the XVIII International AIDS Conference in Vienna, Austria. The workshop will focus on the topic of HIV reservoirs. The persistence of latent HIV reservoirs in different compartments of the body is one of the main barriers to the eradication of HIV infection.



Deadline for Abstract Submission:  
**10 February 2010**  
Submit online at  
<http://www.aids2010.org/>



Abstracts submitted for AIDS 2010 Track A will be considered for the workshop

Designed by: Kaitlin Forrest



"Let's just say that I'm in a mood of cautious optimism."

# HIV Vaccine history

August 1987

1st phase I trial

1987-2007

> 110 trials (10 Phase II/III) with 67 products (27 500 volunteers)



*Candidate vaccine are usually safe and showed some degree of immunogenicity*

2003

Data of the 1st phase III efficacy trial VaxGen



*Lack of efficacy of rgp120 definitively proven*

Sept. 2007

STEP/Phambili phase IIb trial (HIV-1B gag, pol, nef / rAd5)



*Discontinued for lack of efficacy*

Oct. 2009

RV144 "Thai": ALVAC (gag/pol/env) + AidsVax (B/ErGp120)



*Very Modest Efficacy (31%)*

Ongoing phase II trials (DNA+MVA, DNA+NYVAC, lipopeptides...)

# Why it should be possible to obtain an HIV/AIDS Vaccine ?

- Vaccines are effective against other viral diseases
- There is evidence that very few individuals are protected against HIV-1 infection (*e.g. exposed non-infected subjects*)
- Some experimental vaccines confer protection to monkeys infected with SIV
- Recent identification of new neutralizing epitopes using trimeric and/or HIV-1 env
- Certain vaccine candidates may induce immune responses in vaccinees without any major adverse event
- One vaccine prime -boost strategy showed for a first time a modest efficacy (31% of protection in the Thai-RV144 vaccine efficacy trial)



# Global HIV Vaccine Enterprise

Promoting innovation and collaboration to speed the search for an HIV vaccine

The map displays the following logos and flags:

- Canada:** Canadian flag, **iavi** International AIDS Vaccine Initiative, **AVAC** AIDS Vaccine Advocacy Coalition
- USA:** **BILL & MELINDA GATES foundation**, **CVD collaboration** AIDS vaccine discovery, **CHAVI** CENTER FOR HIV/AIDS RESEARCH, **USAID** FROM THE AMERICAN PEOPLE, **HIV VACCINE TRIALS NETWORK**
- UK:** **THE WELLCOME TRUST**, **DFID** Department for International Development
- France:** **gsk**, **sanofi pasteur** The vaccines business of sanofi-aventis Group, **EURORISE**, **EuroVacc**
- EU:** European Union flag, **EDCTP**
- China:** Chinese flag, **anRS** Agence nationale de recherches sur le sida et les hépatites virales
- South Africa:** South African flag, **SAAVI** SOUTH AFRICAN AIDS VACCINE INITIATIVE
- Other:** **Merck**, **National Institute of Allergy and Infectious Diseases**, **DALE AND BETTY BUMPER VACCINE RESEARCH CENTER** NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES NATIONAL INSTITUTES OF HEALTH Vaccines for Life™, **AAYP**, **AIDS Vaccine Asian Network**, **World Health Organization**, **UNAIDS** JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS

**UNAIDS** partners: UNHCR, UNICEF, WFP, UNDP, UNFPA, UNODC, ILO, UNESCO, WHO, WORLD BANK



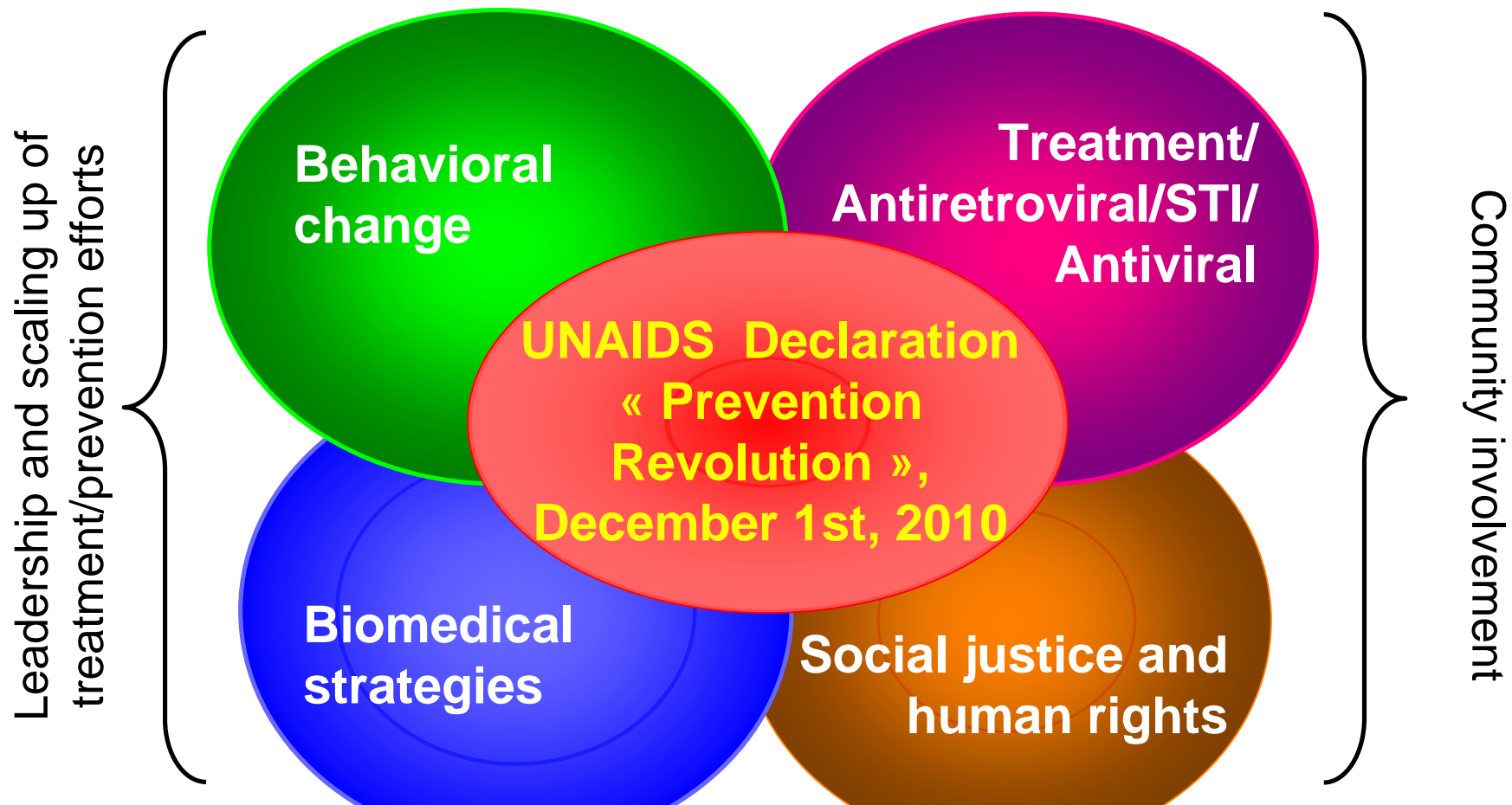
## **10 Challenges of HIV Vaccine R&D**

<b>1.</b>	<b>Unify basic, preclinical and clinical research</b>
<b>2.</b>	<b>Develop data infrastructure for rapid sharing</b>
<b>3.</b>	<b>Bring in new minds and new ideas</b>
<b>4.</b>	<b>Broaden and increase funding</b>
<b>5.</b>	<b>Enhance trial design</b>
<b>6.</b>	<b>Develop world capacity</b>
<b>7.</b>	<b>Engage communities</b>
<b>8.</b>	<b>Assess impact of prevention trial results</b>
<b>9.</b>	<b>Realize potential of non human primate models</b>
<b>10.</b>	<b>Engage industry</b>

## Effectiveness of available tools for prevention..

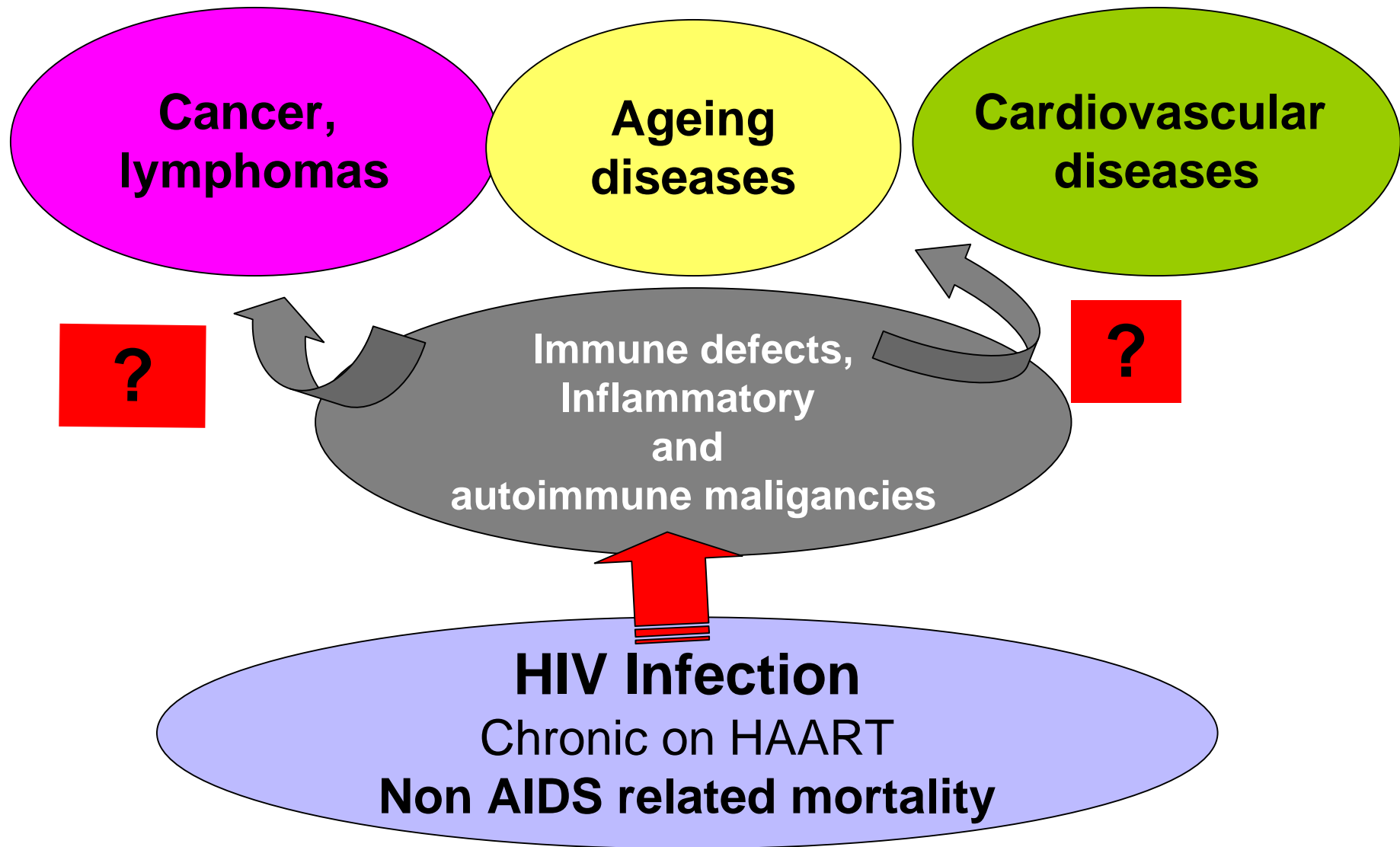
- Condom use : 60-96% (*de Vincenzi 1994 ... Wang 2010*)
- Male circumcision (50-60%, *Auvert 2005, Bailey 2007, Gray 2007*)
- Microbicides using ART (39 -54%, *CAPRISA 2010*)
- PreP in MSM: 44% reduction of HIV incidence (*iPrEx study; NEJM 2010*)
- Needles exchange + fight against discrimination decrease in incidence of HIV among IVDUs in Europe (*Lancet 2010*)
- Decrease in transmission among treated sero-discordant heterosexuals couples (*Bunnel 2007, Sullivan 2009, Del Romero 2010, Donnell 2010*)
- Decrease in prevalence in populations where ART is highly used (*Fang 2004, Montaner 2010, Das 2010, Bezemer 2010*)
- Mathematical models on TASP efficacy (*Granich 2009, Case 2010*)

# Combined prevention strategies to reduce the HIV-1 epidemic...



Call for Universal Policy for Harm reduction, Testing, Counseling, Treating and Assessing for efficacy by monitoring the incidence of HIV infection

# New Challenges: HIV and emerging new diseases...



**Learning from each others beyond HIV/AIDS.....**



# Fighting against HIV/AIDS based on scientific evidences

## A driving force in global health equity

### RISKS PREVENTION

Condom (other STI), clean needles (HCV), Drug injecting facilities (*reduced overdoses, abscesses, skin infections, thrombosis*)

### PMTCT

Contributes directly to 4 of the MDGs where HIV is currently holding back progress (*gender equity & empower women, reduce child mortality, improve maternal health, Combat HIV/AIDS*)

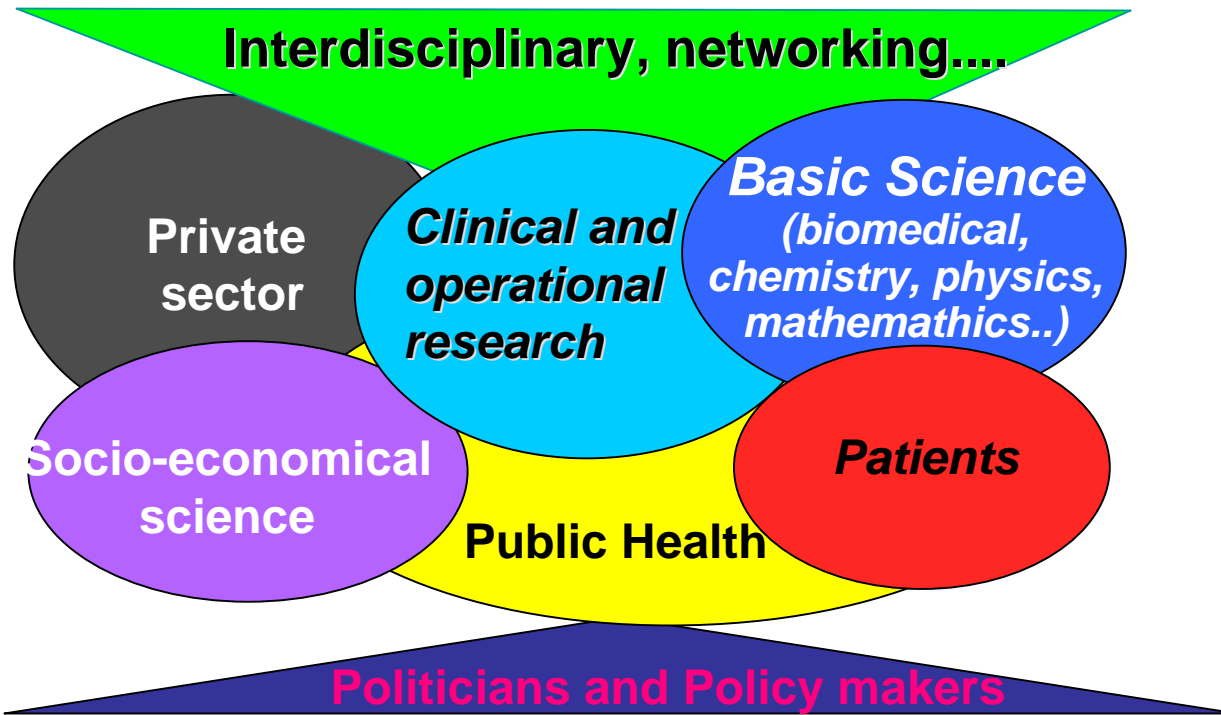
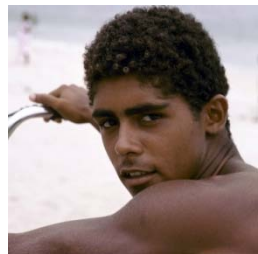
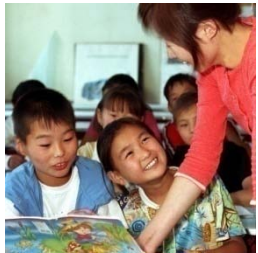
### UNIVERSAL ACCESS TO TREATMENT

Improvements and decentralization of health services, Organization of supply chain, Task shifting, Promote innovative solution for financing health development in resource limited countries (*UNITAID patent pool, tax on financial transaction....*)

### HUMAN RIGHTS

Fighting for an equitable access to care of the most vulnerable and marginalized population (*prostitutes, drug-users, MSM, prisoners...*)

# New discoveries in HIV/AIDS can impact Global Health!



**New challenges, new concepts, new technologies...**

**A new generation of players...**

**But keeping in mind...**

**All together like in the early years!!!**

